

REMARKS

Claims 1, 6, 8, 10, 16, and 45-47 are pending. Claims 1, 6, 8, 16, 45 and 46 stand rejected, and claims 10 and 47 are objected to. Claims 1 and 16 are amended herein to recite that the mature BNP2 polypeptide comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:1. Claims 6 and 45 are amended to recite that the polypeptide comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:1.

In addition, new claim 48 is added. Claim 48 depends from claim 16, and recites that the pharmaceutically acceptable carrier is sterile water, sterile saline, a polyalkylene glycol, an oil of vegetable origin, a hydrogenated naphthalene, lactose, pregelatinized maize starch, polyvinylpyrrolidone, hydroxypropyl methylcellulose, microcrystalline cellulose, calcium hydrogen phosphate, magnesium stearate, talc, silica, potato starch, sodium starch glycolate, or sodium lauryl sulfate.

Support for the amendments presented herein can be found in Applicants' specification at, for example, page 4, line 31 to page 5, line 1; page 8, lines 25-29; page 12, line 23 to page 13, line 10; page 13, lines 20-22; page 14, lines 3-10; and page 18, lines 3-8. Thus, no new matter is added.

In light of these amendments and the following remarks, Applicants respectfully request reconsideration and allowance of claims 1, 6, 8, 10, 16, and 45-48.

Rejections under 35 U.S.C. § 112

The Examiner maintained the rejection of claims 1, 6, 8, 16, and 45, as well as newly added claim 46, under 35 U.S.C. § 112, first paragraph, alleging that they lack enablement, and that a person of skill in the art could not readily make and use the invention as currently claimed without undue experimentation. The Examiner stated that the specification is enabling for a purified BNP2 polypeptide comprising the amino acid sequence of SEQ ID NOS:3 and 36, but alleged that the specification "does not reasonably provide enablement for a structurally and functionally undefined polypeptide comprising an amino acid sequence having at least 91% to 97% identity to the amino acid sequence of SEQ ID NO:1 as broadly claimed." Office Action at

page 3. In response to Applicants' statements filed on April 29, 2010, the Examiner alleged that the specification does not provide sufficient guidance as to "how all the polypeptides comprising fragments and variants with at least 91% or 97% identity to the amino acid sequence of SEQ ID NO:1 . . . are related to the amino acid sequence of SEQ ID NO:3 or 36." Office Action at page 4. The Examiner also alleged that it is unpredictable whether all the claimed variant polypeptides are useful as diagnostic markers, "since there is no guidance to indicate how the variant polypeptides are related to SEQ ID NO:3 or 36." Office Action at page 5.

Applicants respectfully disagree. As amended, independent claims 1 and 16 recite that the mature BNP2 polypeptide comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:1. With respect to the Examiner's statement regarding fragments at page 4 of the Office Action (see above), Applicants note that the present claims recite a mature BNP2 polypeptide.

The present claims are fully enabled. First, Applicants respectfully note that the structural relationship between SEQ ID NO:1 and SEQ ID NOS:3 and 36 was discussed in the response filed on April 29, 2010. In particular, SEQ ID NO:1 lies at the C-terminus of SEQ ID NO:3 and SEQ ID NO:36. This is clearly disclosed in Applicants' specification. *See*, for example, Figure 1A and the description thereof at page 7, lines 2-4 and page 9, lines 5-7. These sections disclose that the sequence set forth in SEQ ID NO:3 is a full-length BNP2 amino acid sequence, that the sequence set forth in SEQ ID NO:36 is a mature BNP2 amino acid sequence (underlined in Figure 1A), and that the sequence set forth in SEQ ID NO:1 is the 33 amino acid C-terminal fragment of human BNP2. Given these teachings, the structural relationship of SEQ ID NO:1 and the claimed polypeptides to SEQ ID NOS:3 and 36 is clear.

Second, Applicants' specification discloses substitutions that can be made within SEQ ID NO:1. For example, Applicants' specification provides sequences for mature BNP2 polypeptides from a variety of species in addition to human. *See*, e.g., Figure 3, which sets forth an alignment of BNP2 amino acid sequences from orangutan, pig, chimpanzee, sheep, mouse, human, gorilla, cat, dog, and snake. Further, SEQ ID NO:20 sets forth a formula (Gly-Xaa₁-Xaa₂-Xaa₃-Xaa₄-Xaa₅-Xaa₆-Xaa₇-Xaa₈-Xaa₉-Xaa₁₀-Xaa₁₁-Xaa₁₂-Xaa₁₃-Xaa₁₄-Xaa₁₅-Xaa₁₆-Xaa₁₇-Xaa₁₈-Xaa₁₉-Xaa₂₀-Xaa₂₁-Xaa₂₂-Xaa₂₃-Xaa₂₄-Xaa₂₅-Xaa₂₆-Xaa₂₇-Xaa₂₈-

Gly- Xaa₂₉- Xaa₃₀- Xaa₃₁- Xaa₃₂) based on the alignment of Figure 3, where the amino acids set forth at each position of SEQ ID NO:20 represent the residues that are present in the naturally-occurring orangutan, pig, chimpanzee, sheep, mouse, human, gorilla, cat, dog, and snake BNP2 polypeptides. Thus, Applicants' specification teaches examples of substitutions that can be made within SEQ ID NO:1.

Further, the Examiner appears to conclude that the only way for the claims to meet the enablement requirement is for the recited polypeptide to be useful as a diagnostic. This is not true. To satisfy the enablement requirement, a specification must enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention, with no undue experimentation. *See*, MPEP § 2164 (citing *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916); *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988); and *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988)).

Applicants' specification teaches that the disclosed polypeptides, including the presently recited polypeptides, can be used to, for example, increase cGMP within a mammal, to dilate an artery within a mammal, or to increase diuresis and/or natriuresis in a mammal. *See*, e.g., the specification at page 5, line 29 to page 6, line 10, as well as page 7, line 25 to page 8, line 14. Applicants' specification further teaches methods for formulating and administering compositions containing polypeptides as recited in the present claims. *See*, page 13, line 11 to page 14, line 13. As such, no undue experimentation would have been required for a person of ordinary skill in the art at the time the application was filed to make and use mature BNP2 polypeptides comprising an amino acid sequence having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO:1, as recited in the present claims.

For at least the reasons presented herein, the present claims are fully enabled. Accordingly, Applicants request withdrawal of the rejection of claims 1, 6, 8, 16, 45, and 46 under 35 U.S.C. § 112, first paragraph.

The Examiner rejected claims 1, 6, 16, and 45 under 35 U.S.C. § 112, first paragraph, alleging that they fail to comply with the written description requirement and that they contain

new matter. In particular, the Examiner alleged that the recitation of “an amino acid sequence having at least 91% or 97% sequence identity to the amino acid sequence of SEQ ID NO:1” was not clearly disclosed in the specification and claims as filed, and changes the scope of the instant disclosure as filed. The Examiner also asserted that the specification only discloses “at least about 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or more percent identity over that length to the amino acid sequence set forth in SEQ ID NO:1 or 2,” and does not teach the claimed genus of polypeptides.

Applicants disagree. To further prosecution, however, Applicants have amended claims 1 and 16 to recite that the polypeptide comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:1, and have amended claims 6 and 45 to recite that the polypeptide comprises an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:1. As indicated by the Examiner (see above), Applicants' specification adequately describes such polypeptides. *See*, for example, page 8, lines 25-29, and page 18, lines 3-8. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1, 6, 16, and 45 under 35 U.S.C. § 112, first paragraph.

Claim Objections

The Examiner objected to claims 10 and 47 as being dependent upon a rejected base claim, but stated that they would be allowable if rewritten in independent form to include all of the limitations of the base claim and any intervening claims.

In light of the amendments and remarks presented herein, Applicants submit that claims 10 and 47 are allowable. As such, Applicants request withdrawal of the objection to claims 10 and 47.

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CONCLUSION

Applicants submit that claims 1, 6, 8, 10, 16, and 45-48 are in condition for allowance, which action is respectfully requested. The Examiner is invited to telephone the undersigned agent if such would further prosecution.

Please apply \$245 for the Petition for Extension of Time fee, \$405 for the Request for Continued Examination fee, and any other charges or credits, to deposit account 06-1050.

Respectfully submitted,

Date: December 21, 2010

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